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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/550,532	09/22/2005	Le T. Duong	21259YP	3180

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EXAMINER	
HUANG, GIGI GEORGIANA	
ART UNIT	**PAPER NUMBER**
1618	
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11/16/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/550,532	DUONG ET AL.	
	Examiner	Art Unit	
	GiGi Huang	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-33* is/are pending in the application.

4a) Of the above claim(s) *7-26 and 33* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6 and 27-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/19/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I in the reply filed on October 12, 2007 is acknowledged. The restriction is traversed on the grounds for meeting burden. This is not found persuasive because the instant application is a 371 national stage application for which the requirement for restriction is not burden, but lack of unity, which has been addressed, in the previous action. The instant case is submitted under 35 U.S.C. 371, the Unity of Invention practice in MPEP §1850 and MPEP §1893.03(d) was followed, not restriction practice. Thus the criteria for burden stated in MPEP §803 for national applications filed under 35 U.S.C. 111(a) does not apply (MPEP §801). As the technical feature did not contribute over the art, the restriction was applied appropriately.

The requirement is still deemed proper and is therefore made FINAL.

Status of Application

2. Applicant has elected Group I in response to restriction requirement for the examination.

Due to restriction, based on election of Group I, claims 7-26 and 33 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

3. Claims 1-6 and 27-32 are present for examination at this time.

Claim Objections

4. Claim 31 is missing a space in the term Claim30". Appropriate correction is required.

Claim Rejections - 35 USC § 112

5. Claims 3-6 and 29-32 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. The term "an integrin inhibitor" is not defined nor adequately described in the specification leaving it open to any and every interpretation of the generic term. It does not allow one of skill in the art to know what precisely in the invention encompasses or allows one of the art to understand what the inventors were precisely in possession of at the time of the invention. The term "an integrin inhibitor" is not adequately described as it is defined by a functional characteristic applicable to many forms of integrins, thereby it is not shown for one of skill in the art to recognize that the applicant was in possession of every aspect of the genus or of the term "an integrin inhibitor" as a result. Thereby "an integrin inhibitor" is described only by a functional characteristic that is not sufficient for written description purposes.

6. Claims 3-6 and 29-32 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. The term "cathepsin K inhibitor" is not defined nor adequately described in the specification leaving it open to any and

every interpretation of the generic term. It does not allow one of skill in the art to know what precisely in the invention encompasses or allows one of the art to understand what the inventors were precisely in possession of at the time of the invention. The term "cathepsin K inhibitor" is not adequately described as it is defined by a functional characteristic thereby it is not shown for one of skill in the art to recognize that the applicant was in possession of every aspect of the genus or of the term "cathepsin K inhibitor" as a result. Thereby "cathepsin K inhibitor" is described only by a functional characteristic that is not sufficient for written description purposes.

7. Claims 3-6 and 29-32 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. The term "selective estrogen receptor modulator" is not defined nor adequately described in the specification leaving it open to any and every interpretation of the generic term. It does not allow one of skill in the art to know what precisely in the invention encompasses or allows one of the art to understand what the inventors were precisely in possession of at the time of the invention. The term "selective estrogen receptor modulator" is not adequately described as it is defined by a functional characteristic thereby it is not shown for one of skill in the art to recognize that the applicant was in possession of every aspect of the genus or of the term "selective estrogen receptor modulator" as a result. Thereby "selective

estrogen receptor modulator" is described only by a functional characteristic that is not sufficient for written description purposes.

For purposes of examination, the "selective estrogen receptor modulator" will be restricted to those described in the specification on Page 8.

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 1-6 and 27-32 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims are drawn to "eliciting a disease modifying effect". The term "eliciting a disease modifying effect" is indefinite as it is unclear to the amount of modification needed for the arthritic condition to be considered adequate to be a "eliciting a disease modifying effect". It could be no improvement, less than1%, or 100% recovery. It does not allow one of skill in the art to the metes and bounds of the invention.

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claims 1-4 and 27-30 are rejected under 35 U.S.C. 102(b) as being anticipated by Whiteford (WO 94/14455).

Whiteford teaches methods of use and compositions comprising bisphosphonates and estrogen. Whiteford teaches the combination therapy comprising two anti-resorptive compounds, estrogen and bisphosphonates, specifically alendronate, for many conditions including age-related bone loss and osteoarthritis. Specific compositions were comprised of estradiol and alendronate (4-amino-1-hydroxybutan-1,1-biphosphonic acid). The effective dose for biphosphonate is preferably about 10ug/kg to about 200ug/kg of body weight, but the precise dosage will vary with the age, size, and severity of the disorder among other factors, which is determined by the caregiver. However, Whiteford teaches that appropriate amounts may be determined by routine experimentation (Page 1, lines 5-12 and 21-27, Page 2, lines 1-5, Page 3, lines 22-30, Page 4, lines 1-35, Page 5, lines 1-13, Page 6, lines 29-36, Page 7, lines 1-35, Page 8, lines 1-15, Page 10, lines 1-30, Page 11).

All the critical elements are taught by the cited reference and thus the claims are anticipated.

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

13. Claims 5-6 and 31-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Whiteford (WO 94/14455) as applied to claims 1-4 and 27-30 above, and in view

of Lehmann et al. (Effect of bisphosphonates on cartilage turnover assessed with a newly developed assay for collagen type II degradation products).

The teachings of Whiteford are addressed above, including the effective dose for biphosphonate, preferably in the range of about 10ug/kg to about 200ug/kg of body weight. The average weight of a female is about 61kg and for males it is 70kg. The resulting ranges are about 6.1 to about 122mg (women) and about 7mg to about 140mg (men). Whiteford does also address that appropriate amounts may be determined by routine experimentation.

Whiteford does not expressly teach the dosage of about 70mg to about 280mg weekly or specifically about 140mg weekly.

Lehmann et al. teaches that bisphosphonates, specifically alendronate, are useful in cartilage turnover found in arthritis, most commonly osteoarthritis. Lehmann also teaches that alendronate was most effective in decreasing CTX-I at 10mg and 20mg daily and most effective (and statistically significant) in decreasing CTX-II at 20mg daily. The total weekly amount at 20mg daily is 140mg.

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to utilize alendronate at 20mg, as suggested by Lehmann, and produce the instant invention. It would have been obvious to utilize the alendronate at 20mg as Lehmann taught that dose was effective for decreasing both CTX-I and CTX-II at statistically significant levels.

One of ordinary skill in the art would have been motivated to do this because as taught by Whiteford, appropriate amounts may be determined by routine

experimentation by one of skill in the art. One would have been motivated to use the 20mg/day (120mg weekly) as it would be desirable to have a level that was effective for decreasing both CTX-I and CTX-II needed to protect cartilage, which as taught by Lehmann, results in decrease osteoarthritis incidence and prevalence. It is also desirable to optimize levels to have greater effectiveness and coverage for as many factors, cascades, and conditions to increase the versatility of a product.

A reference is good not only for what it teaches by direct anticipation but also for what one of ordinary skill in the art might reasonably infer from the teachings. From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Conclusion

14. Claims 1-6 and 27-32 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to GiGi Huang whose telephone number is (571) 272-9073. The examiner can normally be reached on Monday-Thursday 8:30AM-6:00PM EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

GH

MICHAEL G. HARTLEY
SUPERVISORY PATENT EXAMINER